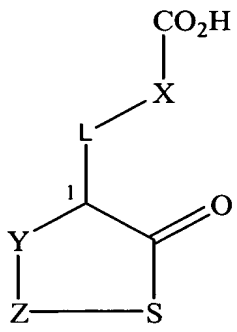
WE CLAIM:

1. A compound of formula I, II or III



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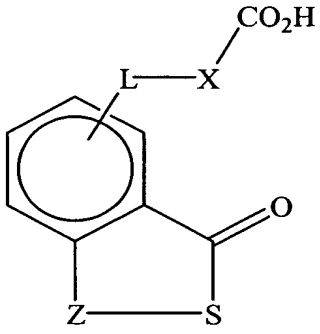

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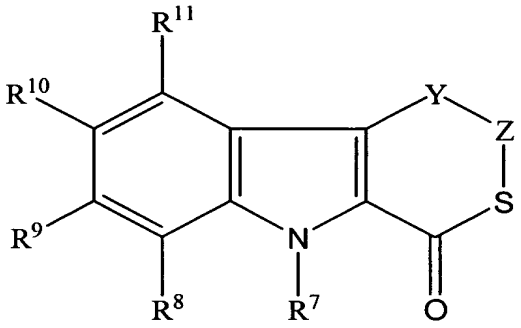


III

or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers of the compound, wherein:

X is C_1-C_4 alkylene, C_2-C_4 alkenylene, C_2-C_4 alkynylene, C_3-C_8 cycloalkylene, C_5-C_7 cycloalkenylene or Ar, wherein the alkylene, alkenylene, alkynylene, cycloalkylene or cycloalkenylene is unsubstituted or substituted with one or more substituent(s);

L is a bond, $-CR^1R^2-$, -O-, -S-, $-SO_2-$ or $-NR^1-$;

Y is -O-, -S-, $-CR^3R^4-$ or $-NR^3-$;

Z is $-(CR^5R^6)_n-$;

n is 1, 2, 3 or 4;

Ar is a bivalent aryl or heteroaryl radical that is unsubstituted or substituted with one or more substituent(s);

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, C_1-C_4 alkyl or C_2-C_4 alkenyl, wherein the alkyl or alkenyl is unsubstituted or substituted with one or more substituent(s);

R^7 is hydrogen, phenyl, phenylethyl or benzyl wherein the phenyl, phenylethyl or benzyl is unsubstituted or substituted with one or more substituent(s); and

R^8, R^9, R^{10} and R^{11} are independently hydrogen, carboxy, hydroxy, halo, nitro, cyano, C_1-C_4 alkyl or C_1-C_4 alkoxy;

provided that when the compound is of formula I, L is a bond and X is ethyl, then Y is not $-CR^3R^4-$.

2. The compound of claim 1, wherein the compound is of formula I.

3. The compound of claim 2, wherein:
Y is $-CR^3R^4-$; and
n is 1 or 2.

4. The compound of claim 3, wherein:
L is $-CR^1R^2-$, -O-, -S- or NH;
X is C_1-C_2 alkylene or Ar; and
Ar is phenylene, biphenylene, benzylene or naphthylene, wherein the phenylene, biphenylene, benzylene or naphthylene is unsubstituted or substituted with one or more substituent(s) independently selected from carboxy, halo, nitro, C_1-C_4 alkyl, , C_1-C_4 alkoxy, phenyl, phenoxy and benzyloxy.

5. The compound of claim 4, which is 3-[(2-oxotetrahydro-2H-thiopyran-3-yl)methyl]benzoic acid or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers thereof.

6. The compound of claim 1, wherein the compound is of formula II.

7. The compound of claim 6, wherein:
L is a bond, $-CR^1R^2-$ or -O-; and
n is 2.

8. The compound of claim 7, wherein:
X is C_1-C_4 alkylene or Ar; and
Ar is phenylene, biphenylene or benzylene that is unsubstituted or substituted with one or more substituent(s) independently selected from carboxy, halo, nitro, C_1-C_4 alkyl, C_1-C_4 alkoxy, phenoxy and benzyloxy.

9. The compound of claim 8, which is:
3-(1-oxo-isothiochroman-8-yl)-benzoic acid;

3-(1-oxo-isothiochroman-8-yloxymethyl)-benzoic acid; or

a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers thereof.

10. The compound of claim 1, wherein the compound is of formula III.

11. The compound of claim 10, wherein:

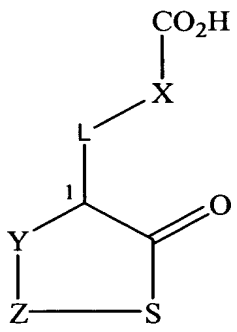
R^8, R^9, R^{10} and R^{11} are independently hydrogen or carboxy.

12. The compound of claim 11, wherein:

R^7 is phenyl or benzyl substituted with one or more substituent(s) independently selected from carboxy, halo, C_1-C_4 alkyl and C_1-C_4 alkoxy.

13. The compound of claim 12 which is 3-(1-oxo-3,4-dihydro-1H-2-thia-9-aza-fluoren-9-yl)-benzoic acid.

14. A method for inhibiting NAALADase enzyme activity, treating a glutamate abnormality, effecting a neuronal activity, treating a prostate disease, treating cancer, inhibiting angiogenesis, effecting a TGF-β activity, treating Huntington's disease, treating diabetes, treating a retinal disorder or treating glaucoma, comprising administering to a mammal in need of such inhibition, treatment or effect, an effective amount of a compound of formula I, II or III



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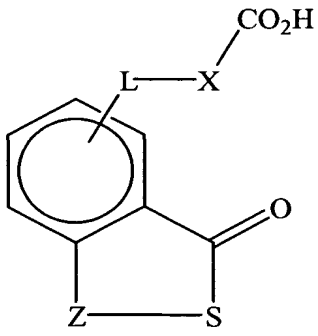

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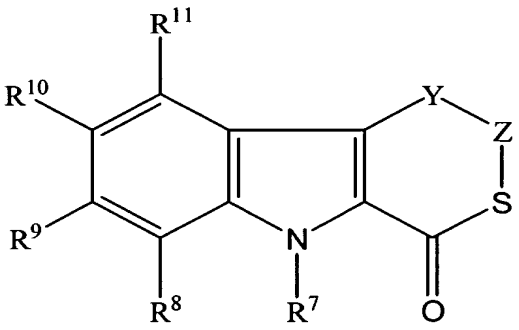


III

or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers of the compound, wherein:

X is C_1-C_4 alkylene, C_2-C_4 alkenylene, C_2-C_4 alkynylene, C_3-C_8 cycloalkylene, C_5-C_7 cycloalkenylene or Ar, wherein the alkylene, alkenylene, alkynylene, cycloalkylene or cycloalkenylene is unsubstituted or substituted with one or more substituent(s);

L is a bond, $-CR^1R^2-$, -O-, -S-, $-SO_2-$ or $-NR^1-$;

Y is -O-, -S-, $-CR^3R^4-$ or $-NR^3-$;

Z is $-(CR^5R^6)_n-$;

n is 1, 2, 3 or 4;

Ar is a bivalent aryl or heteroaryl radical that is unsubstituted or substituted with one or more substituent(s);

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, C_1-C_4 alkyl or C_2-C_4 alkenyl, wherein the alkyl or alkenyl is unsubstituted or substituted with one or more substituent(s);

R^7 is hydrogen, phenyl, phenylethyl or benzyl wherein the phenyl, phenylethyl or benzyl is unsubstituted or substituted with one or more substituent(s); and

R^8, R^9, R^{10} and R^{11} are independently hydrogen, carboxy, hydroxy, halo, nitro, cyano, C_1-C_4 alkyl or C_1-C_4 alkoxy.

15. The method of claim 14, wherein the method is for treating a glutamate abnormality selected from compulsive disorder, stroke, demyelinating disease, schizophrenia, Parkinson's disease, amyotrophic lateral sclerosis (ALS), anxiety, anxiety disorder, memory impairment and glaucoma.

16. The method of claim 15, wherein the glutamate abnormality is a compulsive disorder that is alcohol, nicotine, cocaine or opioid dependence.

17. The method of claim 14, wherein the method is for effecting a neuronal activity selected from stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration and treatment of a neurological disorder.

18. The method of claim 17, wherein the neuronal activity is treatment of a neurological disorder that is pain, diabetic neuropathy, peripheral neuropathy, traumatic brain injury, physical damage to spinal cord, stroke associated with brain damage, a demyelinating disease or a neurological disorder relating to neurodegeneration.

19. The method of claim 18, wherein the peripheral neuropathy is HIV-, chemical- or vitamin-induced.

20. The method of claim 18, wherein the pain is diabetic neuropathic pain.

21. The method of claim 20, wherein the compound is administered in combination with an effective amount of morphine.

22. The method of claim 18, wherein the neurological disorder relating to neurodegeneration is Parkinson's disease.

23. The method of claim 18, wherein the neurological disorder relating to neurodegeneration is amyotrophic lateral sclerosis (ALS).

24. The method of claim 14, wherein the method is for treating a prostate disease that is prostate cancer.

25. The method of claim 14, wherein the method is for treating cancer.

26. The method of claim 25, wherein the cancer is of the brain, kidney or testis.

27. The method of claim 14, wherein the method is for inhibiting angiogenesis.

28. The method of claim 14, wherein the method is for effecting a TGF-β activity.

29. The method of claim 28, wherein the effecting a TGF-β activity is increasing, reducing or regulating TGF- β levels, or treating a TGF- β abnormality.

30. The method of claim 29, wherein the TGF-β abnormality is neurodegenerative disorder, extra-cellular matrix formation disorder, cell-growth related disease, infectious disease, immune related disease, epithelial tissue scarring, collagen vascular disease, fibroproliferative disorder, connective tissue disorder, inflammation, inflammatory disease, respiratory distress syndrome, infertility or diabetes.

31. The method of claim 14, wherein the method is for treating Huntington's disease.

32. The method of claim 14, wherein the method is for treating diabetes that is type I or type II diabetes mellitis.

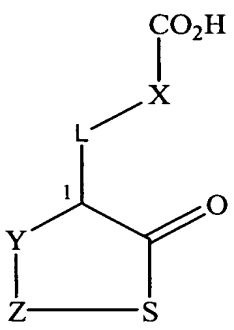
33. The method of claim 14, wherein the method is for treating a retinal disorder that is diabetic retinopathy.

34. The method of claim 14, wherein the method is for treating a retinal disorder that is age-related macular degeneration.

35. The method of claim 14, wherein the method is for treating glaucoma.

36. A method for detecting a disease, disorder or condition where NAALADase levels are altered, comprising:

(i) contacting a sample of bodily tissue or fluid with an effective amount of a compound of formula I, II or III



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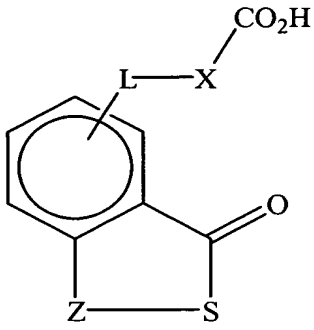

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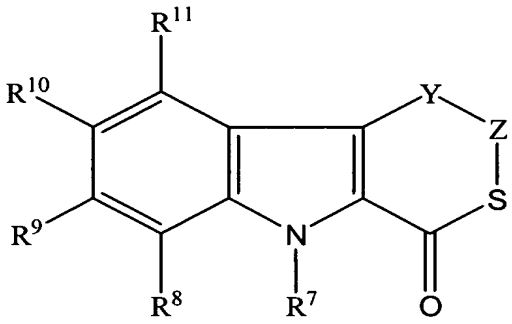


III

or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers of the compound, wherein:

X is C_1-C_4 alkylene, C_2-C_4 alkenylene, C_2-C_4 alkynylene, C_3-C_8 cycloalkylene, C_5-C_7 cycloalkenylene or Ar, wherein the alkylene, alkenylene, alkynylene, cycloalkylene or cycloalkenylene is unsubstituted or substituted with one or more substituent(s);

L is a bond, $-CR^1R^2-$, -O-, -S-, $-SO_2-$ or $-NR^1-$;

Y is -O-, -S-, $-CR^3R^4-$ or $-NR^3-$;

Z is $-(CR^5R^6)_n-$;

n is 1, 2, 3 or 4;

Ar is a bivalent aryl or heteroaryl radical that is unsubstituted or substituted with one or more substituent(s);

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, C_1-C_4 alkyl or C_2-C_4 alkenyl, wherein the alkyl or alkenyl is unsubstituted or substituted with one or more substituent(s);

R^7 is hydrogen, phenyl, phenylethyl or benzyl wherein the phenyl, phenylethyl or benzyl is unsubstituted or substituted with one or more substituent(s);

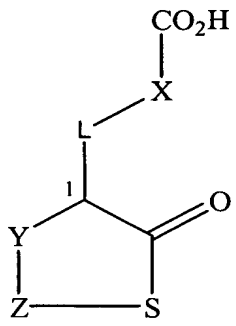
R^8, R^9, R^{10} and R^{11} are independently hydrogen, carboxy, hydroxy, halo, nitro, cyano, C_1-C_4 alkyl or C_1-C_4 alkoxy; and

the compound binds to any NAALADase in the sample; and

(ii) measuring the amount of any NAALADase bound to the sample, wherein the amount of NAALADase is diagnostic for the disease, disorder or condition.

37. A method for detecting a disease, disorder or condition where NAALADase levels are altered in a mammal, comprising:

(i) labeling a compound of formula I, II or III



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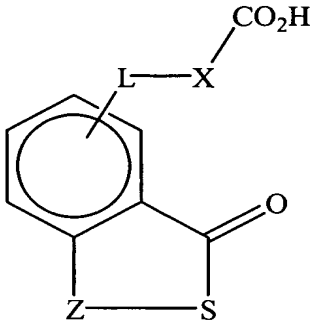

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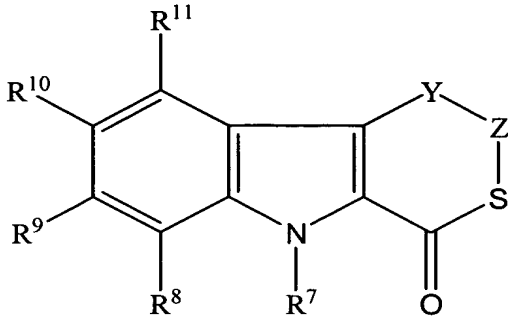


III

or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers of the compound, wherein:

X is C_1-C_4 alkylene, C_2-C_4 alkenylene, C_2-C_4 alkynylene, C_3-C_8 cycloalkylene, C_5-C_7 cycloalkenylene or Ar, wherein the alkylene, alkenylene, alkynylene, cycloalkylene or cycloalkenylene is unsubstituted or substituted with one or more substituent(s);

L is a bond, $-CR^1R^2-$, -O-, -S-, $-SO_2-$ or $-NR^1-$;

Y is -O-, -S-, $-CR^3R^4-$ or $-NR^3-$;

Z is $-(CR^5R^6)_n-$;

n is 1, 2, 3 or 4;

Ar is a bivalent aryl or heteroaryl radical that is unsubstituted or substituted with one or more substituent(s);

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, C_1-C_4 alkyl or C_2-C_4 alkenyl, wherein the alkyl or alkenyl is unsubstituted or substituted with one or more substituent(s);

R^7 is hydrogen, phenyl, phenylethyl or benzyl wherein the phenyl, phenylethyl or benzyl is unsubstituted or substituted with one or more substituent(s); and

R^8, R^9, R^{10} and R^{11} are independently hydrogen, carboxy, hydroxy, halo, nitro, cyano, C_1-C_4 alkyl or C_1-C_4 alkoxy;

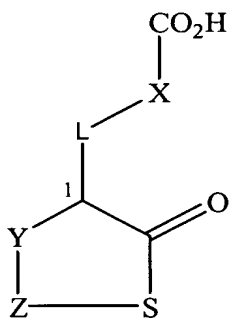
with an effective amount of an imaging reagent;

(ii) administering to the mammal an effective amount of the labeled compound;

(iii) allowing the labeled compound to localize and bind to NAALADase present in the mammal; and

(iv) measuring the amount of NAALADase bound to the labeled compound, wherein the amount of NAALADase is diagnostic for the disease, disorder or condition.

38. A diagnostic kit for detecting a disease, disorder or condition where NAALADase levels are altered, comprising a compound of formula I, II or III



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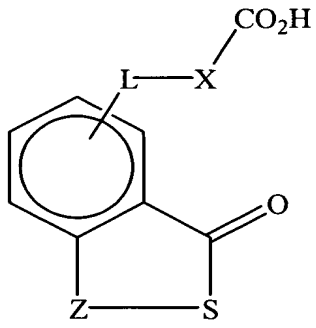

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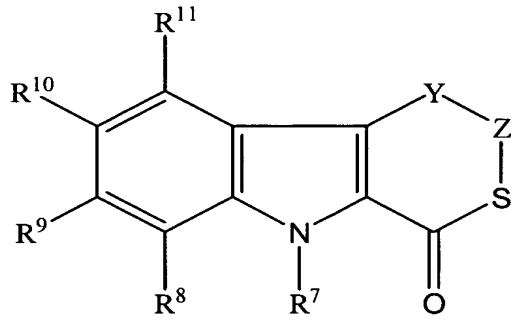


III

or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers of the compound, wherein:

X is C_1-C_4 alkylene, C_2-C_4 alkenylene, C_2-C_4 alkynylene, C_3-C_8 cycloalkylene, C_5-C_7 cycloalkenylene or Ar, wherein the alkylene, alkenylene, alkynylene, cycloalkylene or cycloalkenylene is unsubstituted or substituted with one or more substituent(s);

L is a bond, $-CR^1R^2-$, -O-, -S-, $-SO_2-$ or $-NR^1-$;

Y is -O-, -S-, $-CR^3R^4-$ or $-NR^3-$;

Z is $-(CR^5R^6)_n-$;

n is 1, 2, 3 or 4;

Ar is a bivalent aryl or heteroaryl radical that is unsubstituted or substituted with one or more substituent(s);

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, C_1-C_4 alkyl or C_2-C_4 alkenyl, wherein the alkyl or alkenyl is unsubstituted or substituted with one or more substituent(s);

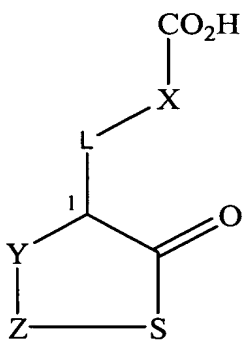
R^7 is hydrogen, phenyl, phenylethyl or benzyl wherein the phenyl, phenylethyl or benzyl is unsubstituted or substituted with one or more substituent(s);

R^8, R^9, R^{10} and R^{11} are independently hydrogen, carboxy, hydroxy, halo, nitro, cyano, C_1-C_4 alkyl or C_1-C_4 alkoxy; and

the compound is labeled with a marker.

39. A pharmaceutical composition comprising:

(i) an effective amount of a compound of formula I, II or III



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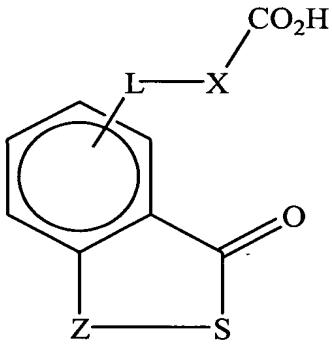

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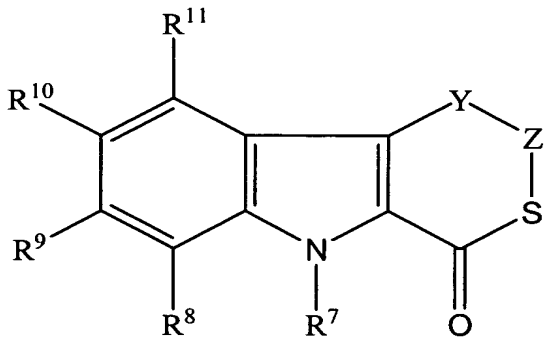

III

or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers of the compound, wherein:

X is C_1-C_4 alkylene, C_2-C_4 alkenylene, C_2-C_4 alkynylene, C_3-C_8 cycloalkylene, C_5-C_7 cycloalkenylene or Ar, wherein the alkylene, alkenylene, alkynylene, cycloalkylene or cycloalkenylene is unsubstituted or substituted with one or more substituent(s);

L is a bond, $-CR^1R^2-$, -O-, -S-, $-SO_2-$ or $-NR^1-$;

Y is -O-, -S-, $-CR^3R^4-$ or $-NR^3-$;

Z is $-(CR^5R^6)_n-$;

n is 1, 2, 3 or 4;

Ar is a bivalent aryl or heteroaryl radical that is unsubstituted or substituted with one or more substituent(s);

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, C_1-C_4 alkyl or C_2-C_4 alkenyl, wherein the alkyl or alkenyl is unsubstituted or substituted with one or more substituent(s);

R^7 is hydrogen, phenyl, phenylethyl or benzyl wherein the phenyl, phenylethyl or benzyl is unsubstituted or substituted with one or more substituent(s); and

R^8, R^9, R^{10} and R^{11} are independently hydrogen, carboxy, hydroxy, halo, nitro, cyano, C_1-C_4 alkyl or C_1-C_4 alkoxy; and

(ii) a pharmaceutically acceptable carrier.

40. A compound which is 3-(2-oxo-tetrahydrothiopyran-3-yl)-propionic acid or a pharmaceutically acceptable equivalent, an optical isomer or a mixture of isomers thereof.

41. A method for inhibiting NAALADase enzyme activity, treating a glutamate abnormality, effecting a neuronal activity, treating a prostate disease, treating cancer, inhibiting angiogenesis, effecting a TGF-β activity, treating Huntington's disease, treating diabetes, treating a retinal disorder or treating glaucoma, comprising administering to a mammal in need of such inhibition, treatment or effect, an effective amount of the compound of claim 40.

42. A pharmaceutical composition comprising:

(i) an effective amount of the compound of claim 40; and

(ii) a pharmaceutically acceptable carrier.